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Disease-a-Month

Chronic and Recurrent Diarrhea

THOMAS P. ALMY

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TO THE general practitioner or the internist, the complaint of protracted diarrhea is significant as an indication of serious disease, as a clue to an underlying personality disorder and as a symptom often disabling in itself. To investigate the possible causes and to apply this knowledge for the patient's benefit, the physician must conduct an orderly and comprehensive study of the patient, combining the technics of ordinary history taking, of psychiatric interviewing and of physical and endoscopic examination, supplemented by the judicious use of a variety of laboratory procedures.

This review will concern itself first with a method of comprehensive diagnostic study in patients with diarrhea. Such a thorough work-up will bring to light a number of conditions in which the criteria of diagnosis and the desirable steps in management are well known and subject to little controversy. It is felt that no good purpose will be served here by a discussion of diarrhea due to specific agents or to carcinoma of the large or small intestine. In our well sanitated communities, most of the difficult cases of chronic or recurrent diarrhea have no recognized basis in pathologic anatomy, and an understanding of these must be based on known and currently postulated mechanisms of disturbed physiology of the

intestines. In others with recognizable intestinal lesions, the associated functional disturbances are likewise important to the mechanism of symptom production and in rational management. For these reasons, pathologic physiology is here emphasized—first in relation to diarrhea in general, later in consideration of certain common clinical entities.

ETIOLOGY

The possible causes of chronic and recurrent diarrhea are numerous. The following classification is necessarily incomplete, but it will serve as a check list and as a criterion for adequacy of the diagnostic survey.

I. *Functional disorders*
   - A. Nonspecific reaction to stress—psychogenic or psychosomatic diarrhea—mucous colitis
   - B. Allergy to ingested foods
   - C. Defects in dietary intake
     1. Vitamin deficiency—pellagra
     2. Overuse of coarse or irritating food
   - D. Defective digestion—pancreatogenous steatorrhea
   - E. Defective absorption—sprue or idiopathic steatorrhea
   - F. Overuse of cathartics

II. *Intrinsic disease of the intestine*
   - A. Inflammatory
     1. Due to pathogenic bacteria—Shigella sp., Salmonella sp., Mycobacterium tuberculosis hominis et bovis, etc.
     2. Due to pathogenic fungi—e.g., Histoplasma capsulatum
     3. Due to viral agents—e.g., lymphogranuloma venereum
     4. Due to protozoa—chiefly Endameba histolytica
     5. Due to helminths—such as Strongyloides stercoralis, Schistosoma mansoni or S. japonicum
     6. Nonspecific inflammatory diseases—regional enterocolitis, ulcerative colitis, diverticulitis
     7. Untoward effects of broad spectrum antibiotics, with alteration in fecal flora
   - B. Neoplastic
     1. Benign tumors—adenoma (polyp), leiomyoma, lipoma
     2. Malignant tumors—carcinoma, lymphosarcoma or Hodgkin's disease, sarcoma.
   - C. Operative or postoperative fistula formation—gastrojejunostomy, ileocolostomy, gastrojejunocolic fistula

III. *Extrinsic disease affecting the intestine*
   - A. Disease of the nervous system, such as tabes dorsalis or any cerebral lesion causing increased intracranial pressure

B. Advanced renal insufficiency
C. Endocrinopathies—Graves' disease and Addison's disease
D. Passive congestion of the intestines in cardiac decompensation, cirrhosis of the liver or portal vein thrombosis

A MODUS OPERANDI

The foregoing list cannot be applied directly to the workaday problems of clinical diagnosis—it is too long to be remembered. In a given case, diarrhea is less often due to one specific cause than to multiple etiologic factors; these must be separately identified and their relative significance estimated. Further, we recognize increasingly that the body can respond only in a limited number of ways to a host of environmental stimuli. Hence the physician often fails to reach a final conclusion regarding the cause of diarrhea from the history and bedside examination. In most cases, nevertheless, the history does provide the essential clues to a preliminary formulation and reduces the list of etiologic possibilities to a more workable size. These clues are related to the *location* and the *nature* of the disease process.

The location of the underlying disorder within the bowel is suggested by the character of the stools and by the location and quality of any accompanying pain. It is convenient to distinguish between *large-stool diarrheas* and *small-stool diarrheas*. When the stools are consistently large, the underlying disorder or disease is likely to be in the small intestine or the proximal colon. The diarrhea is thought to result from the stimulation of a functionally normal colon (or distal colon) by exceptionally large or unusually irritating intestinal contents. The stimulus thus presented is similar to that of an enema, leading to expulsion of loose stools of large size despite the normal irritability of the lower bowel. Such stools are likely to be light in color; to be watery, frothy, soapy or greasy; to be foul; to be free of gross blood, and to contain undigested food particles. When pain accompanies this large-stool diarrhea, it is likely to be periumbilical in location or localized in the right lower quadrant. These areas have been recognized, both by clinical and by experimental evidence, as the zones of pain reference from the mesenteric small intestine and the cecum. The pain in such instances is often intermittent, cramplike and accompanied by audible borborygmi.

In small-stool diarrhea the patient frequently has urges to defe-

cate but passes abnormally small quantities of feces. In its extreme form he may, despite a great sense of urgency, pass only flatus or a small quantity of mucus. This syndrome is likely to be associated with disease or disorder of the left half of the colon and the rectum, and is thought to develop because the reservoir function of that segment has been impaired. This increase in the irritability of that section results in the premature discharge of a quantity of stool otherwise insufficient to trigger a defecation reflex. When fecal matter in any quantity is passed, it is mushy or jelly-like; it is sometimes admixed with visible mucus or blood; it is usually dark in color, and rarely foul. Pain, when present, is likely to be in the hypogastrium, or in the left or right lower quadrant, or in the sacral region, reflecting the established zones of pain reference from the colon and rectum. It is usually griping, aching or with a quality of tenesmus. It may be continuous; but it usually is relieved to some extent by an enema, a bowel movement or even the passage of flatus.

These two patterns of diarrhea are, of course, not mutually exclusive. With widespread inflammation or dysfunction of the intestines the two mechanisms may occur in the same patient, and even on the same day.

By considering the presenting symptoms in this manner, the probable site of the disease process can be judged and the clinical and laboratory examination of the patient can be better planned. At times this clinical discipline is helpful in correcting errors or omissions in a supposedly complete work-up. Witness the following case:

Mrs. M., a 48 year old, twice-married housewife, complained of diarrhea for 1½ years, with increasingly frequent episodes of cramping abdominal pain. She was entering the menopause and seemed emotionally labile, rigid and compulsive in behavior and under continued tension because of concern over two sons recently returned from military service. Physical examination, including proctosigmoidoscopy, revealed no pertinent findings. Two stools were negative for occult blood and free of amebae on microscopic examination. The BMR was + 5 per cent. A barium enema and x-rays of the esophagus, stomach and duodenum were negative. A diagnosis of mucous colitis was made, and the patient treated by simple psychotherapy, low residue diet and anticholinergic drugs. After eight weeks there was no improvement and her history was reviewed with her. She now disclosed that all of her stools were large and watery and that her pain was periumbilical, sometimes migrating to the right lower quadrant. Since

these facts implicated the mesenteric small intestine, the gastrointestinal series was repeated, with special views of the lower small bowel. These revealed several dilated loops of ileum, with delayed passage of barium in this region. At laparotomy, a lipoma was found in the distal ileum, narrowing the lumen to a diameter of less than 1 cm. This was resected, resulting in complete and lasting relief of her intestinal symptoms.

The history usually supplies valuable information about the *nature* of the disorder or disease process, which can later be substantiated by objective study. It is assumed that the mature clinician will be influenced in his judgment by the duration of the symptoms, their mode of onset and their variable occurrence or progression in severity, and by the age of the patient when the symptoms began. On the other hand, three features of the history, to which special significance is often attached, are in my opinion commonly misinterpreted. *Weight loss* in association with diarrhea is not always indicative of serious underlying organic disease. With small-stool diarrhea of whatever cause, the nutritional loss is not great unless the appetite is impaired. With both mucous colitis and colon cancer, the leading cause of weight loss is likely to be anorexia. The *intensity of pain* may bear no relation to the seriousness of the underlying disease; nor should the relief of pain by a placebo be used as evidence that the disorder is of functional origin. The occurrence of *diarrhea at night* does not always reflect an organic lesion of the bowel.

The probability of *exposure to infectious agents* must be carefully weighed. Mere note that the patient previously resided or traveled in tropical or unsanitary areas leaves many questions unanswered. The duration of exposure and the precautions taken should be understood. Some parasites die off in a few years, while other species outlive the host—so the date of last possible exposure may be important. Some diseases, such as schistosomiasis, are sharply limited to certain geographic areas; while others, such as amebiasis, are of worldwide distribution. With amebiasis, shigellosis and other infections directly transmitted from hand to mouth, a history of residence in a jail, a mental hospital or other public institution may be more significant than one of tropical travel.

The significance of *allergy* as a cause of diarrhea remains controversial. When diarrhea is associated with intestinal bleeding, acute arthropathy and purpura (Schönlein-Henoch purpura),

allergy to ingested food or drugs may be properly suspected. Recurrent diarrhea of the watery large-stool variety, with abrupt onset 30–90 minutes after eating and lasting 6–24 hours, may also be related to ingested foods. These episodes may be marked by periumbilical pain and vomiting. The causation of the sprue syndrome (see below) by wheat gluten may be an example of diarrhea due to allergy. Other diarrheal syndromes seem very rarely to be related to allergic mechanisms. In all such cases the suspicions aroused from personal and family histories of allergic symptoms and from evidence of contact with suspected allergens in foods or medications must be confirmed by food diaries or elimination diets. Skin tests do not suffice to establish such a diagnosis.

The diagnosis of diarrhea as a *reaction to stress* should be made with great care. Even the typical clinical syndrome of mucous colitis, in which small-stool diarrhea is interrupted at times by brief constipation and is associated with dyspepsia and vasomotor instability, may be seen in amebiasis or in carcinoma of the sigmoid. The diagnosis of a psychosomatic mechanism of diarrhea is not to be based entirely on the recognition of typical symptoms and the exclusion of primary organic disease of the bowel, although both of these steps are essential. It is also necessary to demonstrate that the disorder began or recurred at a time of emotional conflict, engendered by some situation of understandable importance to the patient. To do this, the physician must have soundly appraised the personality structure of the patient and must be well informed regarding the events of his personal and family life.

These things require the taking of a *personal history,* which is recommended as a routine in cases of chronic or recurrent diarrhea. Much information of value can be obtained casually as the patient reviews his complaints, provided he is allowed to tell the story in his own way and to include what seem at first to be irrelevant details. Facial expressions, blushing and weeping, or unwillingness to discuss certain events may quickly indicate to the observant physician the nature and causes of emotional conflict in the patient. It is wise, nevertheless, to include in the initial history a brief, systematized inquiry into the more important interpersonal relationships of the patient's life: those with parents, siblings, schoolmates, teachers, employers and co-workers, sexual and marital partners, children and in-laws. Whenever, in discussing these relationships,

the patient evinces some emotion, the subject can be pursued or can be noted for further inquiry at a later date.

In general, patients with diarrhea as a reaction to stress usually have lacked for parental affection, either because of neurosis in the parents or because of their death, divorce or separation. Such patients often appear immature and dependent, rigid and compulsive. Although outwardly pleasing and even apologetic, they often have deep-seated and sustained feelings of guilt and hostility, neither of which finds ready expression in words or actions.

The following case illustrates these elements in the diagnosis.

Mrs. J., aged 47 years, complained of diarrhea for five years. When she was only three months old, her mother was removed to a sanatorium, where she died of tuberculosis five years later. Mrs. J. was reared in her grandmother's home. When her father remarried, she saw little of him because her stepmother frequently beat her. At age 17, against her father's wishes, she married a man twice her age, who turned out to be a gambler and a drunkard. At 18, during her first pregnancy, she developed constipation, vomiting, nausea and right upper quadrant pain. All these symptoms continued during and between pregnancies, which recurred yearly until, eight years later, her husband died of pneumonia following an alcoholic debauch. At age 30, she began to have bouts of diarrhea and lower abdominal pain, punctuating her continued constipation. Diarrhea became more frequent when, at age 39, she was again married to an ineffectual man and acquired two grown stepdaughters, with whom she had almost continual altercations. She came to find her chief comfort in depending upon her eldest son, now grown to manhood. Three years later, this son was killed during military service. Her severe and continued diarrhea began within two hours of the receipt of news of his death. This history, together with subsequent physical and laboratory examinations, was considered to indicate a diagnosis of mucous colitis, and her symptoms were controlled by supportive psychotherapy in a manner to be presented later in this review.

Examination of the Patient

So numerous are the possible causes of diarrhea, and such is the relative importance of the history in the diagnosis, that only rarely does the most complete physical examination yield unexpected diagnostic features. No attempt will be made here to catalogue all the findings to be sought. It is assumed that the severity of illness and of weight loss will be estimated and that mucous membrane lesions, pallor, edema and other signs of specific nutritional deficiency will be noted. Signs of Graves' disease, including warm moist

skin, tremor, goiter and eye signs, should be looked for. Pulmonary findings may suggest the presence of tuberculous enteritis or pancreatogenous steatorrhea. Gaseous distention of the abdomen commonly occurs with diarrhea of small intestinal origin and sometimes with obstructing colonic cancers. The significance of localized abdominal masses or tenderness is well known. Clubbing of the fingers is commonly found in chronic debilitating diarrhea, in the absence of pulmonary disease.

Digital rectal examination and anoscopy often reveal complications (hemorrhoids, anal ulcer) of the diarrheal disorder but seldom disclose its basic nature. Proctosigmoidoscopy, however, often permits visualization of lesions, such as tumors or ulcerative colitis, directly responsible for the complaint. Although there is good reason to believe that spasm and engorgement of the sigmoid colon comprise part of the physiologic basis of mucous colitis, the recognition of such changes by endoscopy does not in itself justify a diagnosis of a "functional disorder." The same gross appearance may be produced by inflammatory changes due to pathogenic bacteria, amebae or cathartics. Furthermore, such changes may occur during emotional tension brought on entirely by the experience of undergoing a proctoscopy.

In the patient with diarrhea, proctosigmoidoscopy can and should be done at the time of the initial physical examination, without preliminary cleansing of the bowel. When fecal matter is encountered, specimens can be promptly obtained for gross inspection, tests for occult blood, culture and warm-stage examination for amebae. Liquid material can be conveniently aspirated with a serological pipette, joined by a length of rubber tubing to a mouthpiece of glass tubing plugged with cotton. If formed stool is encountered, the bowel can be cleansed at once by an enema of hypertonic phosphate solution (provided in disposable containers as Clyserol and Fleet Enema). The importance of prompt endoscopic examination lies, not only in the direct diagnostic aid it provides, but in the increased safety and effectiveness of further steps in management. Except when a carcinoma has been seen or strongly suspected, the indicated microscopic studies and cultures of the stool should be completed before barium is introduced. In any case, barium enema should not immediately follow the proctoscopy, on the same day, because the air introduced at proctoscopy

causes confusing shadows on the films. Most important is the avoidance of castor oil and soapsuds enemas as preparation for x-ray studies in those individuals who have inflammation or partial obstruction of the distal colon.

The diagnostic value of the barium enema depends mainly on thorough cleansing of the bowel, fluoroscopic observation and spot film technic. Any feces or retained air makes the exclusion of small lesions difficult. The overlapping of the loops of bowel, especially in the sigmoid region, makes the use of minimal amounts of barium, positioning of the patient before the fluoroscopic screen, and spot film examinations most important. As haustral markings are often absent in the descending colons of healthy persons studied by barium enema, this finding alone should be considered as only suggestive and not diagnostic of ulcerative colitis. Finally, it should be remembered that the barium enema frequently fails to reveal lesions of the rectum and lower sigmoid. It is the clinician's responsibility, not the radiologist's, to insure that this critical area has been entirely covered by endoscopic or x-ray examinations, even if these must be repeated.

When the basis for the diarrhea is still undiscovered or is not fully defined by the studies already described, x-rays of the stomach and small bowel are indicated. Here it is necessary to be certain that all of the jejunum and ileum have been visualized. The terminal ileum is the site of many disease processes; and in order to see it clearly, it is wise to compare the later films of the gastrointestinal series with those from the barium enema which show an "ileal leak."

No further routine laboratory studies can be recommended for cases of diarrhea beyond the usual urinalysis, complete blood count and sedimentation rate. In most cases of protracted large-stool diarrhea, bedside observations dictate additional studies of the state of nutrition of the patient, outlined below in the section on sprue.

MANAGEMENT OF SPECIFIC TYPES OF CHRONIC DIARRHEA

The symptomatic management of diarrhea often appears strikingly successful in cases of acute, self-limited disease such as infectious enteritis or food poisoning. In such cases, rest, restriction of

food intake and the administration of opiates, bismuth, kaolin or pectin products are usually followed by prompt improvement. One cannot object to the use of these measures for brief periods in cases of chronic or recurrent diarrhea, but the results obtained are often disappointing. Better therapy depends on the recognition of specific disease entities or functional patterns and utilizes methods developed separately for each of these.

Mucous Colitis (Irritable Colon, Psychosomatic Diarrhea)

The diarrhea due to mucous colitis is recognized as a bodily reaction to stress, an accompaniment of emotional tension, similar to the blushing and weeping with which it is sometimes associated. The symptom complex (small-stool diarrhea) indicates that the distal colon is the end organ mainly concerned in the disorder. It is believed that the pathway by which the colonic response is evoked includes the autonomic (parasympathetic) nervous system; and so direct topical stimulation of the colonic mucosa, as by food residues, is of lesser importance. The most important procedure in the management of such patients is *simple psychotherapy*. To be helpful, however, the desired quality of such therapy must be well understood, and the technics used must be chosen to suit the needs of a given patient at a given time.

Patients with diarrhea due to mucous colitis seem *immature* in their social orientation, with *feelings of inadequacy* in the face of personal problems, and unduly *dependent* upon others. The history usually discloses one or more strong dependent relationships—to a single individual at a time (a parent, other relative, friend or teacher)—which have for various reasons become unavailable to the patient and have been broken off. It follows that the physician may most rapidly relieve his patient's emotional tension, and the attendant diarrhea and other symptoms, by allowing the patient to confide in him and depend deeply upon him. This involves no more than the conscious exploitation, for the patient's benefit, of the traditional relationship of patient to doctor and of the words and actions which pass between them. It begins with the manner of history taking, in which the patient is encouraged to tell his story in his own words, with a minimum of interruption. The inclusion

of a simple personal history, as described previously, signifies to the patient the physician's broad concern for his welfare. Yet the patient should not be pressed to reveal his emotional conflicts more rapidly than he chooses to—such revelations must arise naturally out of confidence in the physician's sustained interest, lest the patient again feel abandoned to face these problems alone. It is wise to interrupt any such discussion and divert it to another topic whenever sobbing or other indications of strong emotion are observed. The subject can be reopened at a later visit, when the patient's spirits and self-confidence seem higher.

The thoroughness of the physical examination, in addition to its direct diagnostic importance, signifies to these patients that their problems are being taken seriously and that their doctor has not leaped to a diagnostic conclusion. This secondary value is greater if the examination is completed at the first visit. At that time the patient can be *provisionally reassured* ("I am 99 per cent sure," etc.) that his condition is not dangerous or disabling, after which the necessary laboratory procedures are outlined. The several visits necessary for the conduct of these procedures can be utilized for further brief discussions of elements of significance in the personal history. It is wise to direct each of these interviews toward the illumination of a single subject (for example, the mother-in-law, or the son away from home).

After the evidence from laboratory procedures is assembled, a *definitive formulation* of the illness should be given, together with *strong reassurance* of its benign nature and of the physician's continued interest. The patient will only be confused by the statement that there is "nothing wrong" with him; he will be both confused and humiliated by the term "neurosis" or by any complicated explanation of his illness which indicates that his reactions to stress are weak or atypical. Such insight seldom gives real comfort to the patient with diarrhea, who often regards a statement of this kind as the premise on which the physician denies future responsibility for his welfare. He needs to feel that his troubles are not "his fault" and that he will both require and receive further help from his doctor.

I therefore recommend, in the patient's interest, a formulation actually at variance with demonstrable fact—he should be told that his colon itself is overly reactive to many influences, and

assured that further steps will be taken to help him live comfortably with it. This serene sense of detachment may be compared with that under which many patients view certain distressing orthopedic conditions ("trick knee" or "bum back"), and will provide the background for the subtle, sustained use of many psychotherapeutic resources, with the ultimate aim of strengthening the independence and self-reliance of the patient.

Though the methods used in such continuing psychotherapy need be greatly individualized, certain general principles can be suggested. Initial efforts should be directed at lessening recognizable sources of stress. Physical rest is helpful but less important than release from conflicting obligations—a relative may be induced to accept one of the children for an extended visit, or the patient may resign temporarily from one or more committees or from other work of marginal importance to him. The sources of friction with other members of the family (minor alcoholism in the husband or misinformation on sexual matters) may require understanding and explanation. The patient's true abilities—athletic, manual or intellectual—need to be assayed, and suitable outlets arranged for them—golf, bowling, hobbies, "do-it-yourself" activities, reading and active or passive enjoyment of music. These activities provide further reassurance of general physical capability and help to build self-confidence.

Throughout this treatment the original formulation of the illness to the patient should be kept in mind, and supplementary measures used which are directed at the colon itself. The *diet* prescribed should be free of strong seasoning and of cold fluids; further rules are best devised from the experience of the patient, who is asked to report and discuss his suspected difficulties with food irritants as these occur. Since there are usually few of these, the patient comes to recognize how much he can eat, and to congratulate himself thereon. The use of *placebos* can be fully endorsed, both because placebos have been shown experimentally to have physiologic effects and because of the many records of therapeutic success in this disorder with drugs later proved to be inert in the dosage used. The choice of a placebo is determined largely by the previous medical experience of the patient. It is better to choose an agent he has never before received. He is likely to be too sophisticated for lactose or tincture of gentian, but any of the common "antispasmodic"

agents will be acceptable (unless he critically reads the literature of clinical pharmacology!). The writer's choice is 10–15 drops of tincture of belladonna before each meal and at bedtime. Any of the synthetic "antispasmodic" agents (anticholinergics) may be substituted. *One* tablet of any of these, as commonly marketed, probably has no regular pharmacologic effect on the hyperactive human colon, as revealed in experimental studies. Mild barbiturate *sedation,* as with phenobarbital 15 mg. four times daily, also has placebo value, but the narcosis from larger doses may be harmful.

At times of violent diarrhea, the patient may be helped by lying flat in bed with a hot water bottle or a heating pad on the abdomen, or by soaking for half an hour in a tepid tub. At such times, his acute distress may justify the use of codeine or morphine, orally or hypodermically. Continued use of opiates in any form is to be condemned, chiefly because the illness is a chronic one and habituation a danger, but also because these agents cause continued spasm and engorgement of the colon.

This program of therapy, of course, is only a distillate of crude clinical experience. It is potent to the degree in which it relieves the patient's feelings of fear and helplessness and improves his capacity to adapt to general stress. Improved treatment now awaits a fuller understanding of the bodily mechanisms linking emotional tension to diarrhea. As propulsive movements can be produced in the empty human colon by acetylcholine or methacholine, it is possible that the immediate stimulus to diarrhea is a parasympathetic (cholinergic) discharge. For this reason, a fully active dosage of anticholinergic drugs is recommended during periods of maximum colonic activity. Methantheline bromide (Banthine) 100–150 mg. or propantheline (Probanthine) 45–60 mg. is given at bedtime and on arising. Dosage must be at least enough to dry the mouth or blur vision, side effects which are of little consequence to the patient during sleep. While this measure has been found useful in many patients, it does not fully control the disorder. It is expected that better control will come from an understanding of the central integrating mechanisms related to diarrhea, comparable to those centers concerned with gastric secretion which have recently been found in the hypothalamus.

The prognosis in each case of mucous colitis must be carefully estimated, to provide realistic goals for therapy. As White, Cobb

and Jones have suggested, these patients may be divided at the outset into the "more neurotic" and the "less neurotic" groups. The "less neurotic" patient usually presents a clear temporal relationship between recognizably stressful life situations and the onset and recurrences of diarrhea. In the intervals between these stresses, he is free of symptoms, or nearly so. It follows that his capacity to adapt to ordinary situations is adequate. It is with this group of patients that the time of the practitioner or internist can profitably be spent, with expectation of some lasting benefit. "More neurotic" patients should be treated at first in the same manner, until the experience of at least several weeks confirms initial judgment. At this point, young patients with brief histories of diarrhea (a year or less) should be referred to a psychiatrist, and the remainder treated merely for the direct relief of symptoms.

Nonspecific Ulcerative Colitis

In 95 per cent of all cases the earliest and most severe lesions of ulcerative colitis lie in the distal colon. This location is suggested by the characteristic symptoms: small-stool diarrhea, with visible blood and mucus in the stool in large or small amount and, at times, with low abdominal pain. The disease may begin insidiously or in fulminating fashion. In nearly half the cases the onset is marked by rectal bleeding alone, and diarrhea may not appear until months or years later. Such patients, inadequately examined, are often treated for hemorrhoids.

The diagnosis of ulcerative colitis is usually provided by proctoscopic examination. In the rectum and lower sigmoid the inflammation of the mucosa is diffuse; early cases seldom show any discrete ulcers. The minimal change is *increased friability* of an otherwise normal-appearing mucous membrane: when the mucosa is swabbed with a dry cotton pledget, it becomes intensely red, pours out minute droplets of mucus and oozes blood. In more advanced stages, the mucosa is a deep dull pink, opaque and velvety, and covered with variable amounts of grayish mucus which is often coagulated into a thin reticulum or streaked with blood. In severe acute disease, the folds of mucosa may appear markedly swollen or blood may ooze rapidly from the entire denuded mucosal surface and obscure the field.

As soon as these conditions are seen, the surface exudate should be aspirated for warm-stage examination for amebae and for culture for bacterial pathogens, chiefly Shigella. During the next few days, two or three freshly passed stools should provide additional material for parasitologic study and for a repeat bacterial culture, and a Frei test should be performed. By these means it can be decided whether specific microbial pathogens play a role in etiology. If one of these agents is found, appropriate chemotherapy should certainly be given, but it should not be concluded uncritically that this is the sole cause of the colitis. The treatment of ulcerative colitis as a specific bacillary or amebic infection without first isolating the causative organism is, in the writer's opinion, not justified.

After the complete study of the stools, barium enema should be done and small bowel x-rays taken, to estimate the present extent of the disease and its severity. Care must be taken that preparation for barium enema with castor oil and soapsuds enema, which is routine in many institutions, be canceled. If any cleansing is needed, a gentle warm tap water enema will usually suffice. In early mild cases there may be no x-ray signs, and in advanced disease the lesions almost always involve more of the bowel than the x-rays would indicate. Hence, they serve chiefly as a base line for future comparisons.

Although the etiology of nonspecific ulcerative colitis cannot be regarded as fully established, an effective program of therapy can be offered, based on a synthesis of many facts and some speculations as to the cause.

PSYCHOTHERAPY.—The concept that ulcerative colitis is an adaptive reaction to general stress is supported by highly suggestive but inconclusive evidence. The onset and recurrences of the disease commonly coincide with stressful life situations which evoke characteristic emotional conflicts. In these respects, patients with ulcerative colitis are strikingly similar to those with diarrhea due to mucous colitis; yet, in the former disease the degree of regression or immaturity is often extreme and schizophrenic reactions not uncommonly occur. The motor activity of the colon in ulcerative colitis can be briefly reproduced in the healthy human subject, either by stressful and emotionally significant experimental procedures or by injection of methacholine or acetylcholine. Prolonged

and intensive administration of mechacholine to dogs results in hemorrhagic and inflammatory changes in the colonic mucosa, which are, however, not severe or self-perpetuating.

For these reasons, emphasis is placed on supportive psychotherapy, and some benefit is expected from the intensive use of anticholinergic drugs. All of the concepts and procedures suggested for the management of mucous colitis are appropriate here, with certain quantitative differences. The acutely ill patient rapidly develops an appearance of childish immaturity—he is clinging, demanding, petulant, tearful, seeming at times to be needlessly soiling himself. It is wiser, at the beginning, to accede to his demands and treat him like a child, even though this may involve extreme measures; cases are recorded in which for a time an adult patient was fed formula from a bottle, being held in the arms of a nurse. In most instances the strong supportive role of the physician can be established by multiple brief visits concerned with bodily comfort and bodily needs of the most primitive sort. Double value is gained by the physician who personally orders or obtains specific foods desired by the patient; this symbolizes parental solicitude (as did the bottle feeding mentioned above) and insures the highest level of nutrition for most patients in the acute stage. Similarly, double benefits accrue from good bedside nursing, with attention to creature comforts, such as back rubs and hot water bottles. In hospital practice, even in public wards, it has been found best to assign the major roles in this supportive program to one physician and one nurse, in order to intensify the spirit of *personal* solicitude for the patient. The intensive use of short-acting barbiturates and of anticholinergic drugs in the manner outlined for mucous colitis may serve to diminish stimulation of the colon during continued emotional tension.

TREATMENT OF THE INFECTION.—Whatever the inciting mechanism, the patient with ulcerative colitis presents for treatment a tremendous inflammation, a massive, gangrenous, infected "wound." The "exudate" (stool) contains large amounts of serum, with masses of red blood cells, leukocytes and the bacteria which ordinarily inhabit the colon, the numbers of gram-positive organisms being disproportionately increased. Since the bacteria present are basically nonpathogenic, little can be expected of antibiotic therapy. It can reduce the numbers of organisms for brief periods;

for acutely ill patients penicillin (1,000,000–2,000,000 units) and streptomycin (1.0 Gm.) should be given in divided doses each day for from one to three weeks. Less complete but more lasting suppression can be achieved with oral sulfonamides such as phthalylsulfathiazole (Sulfathalidine) 1.5 Gm. four times daily, or salicylazopyrine (Azulfidine) 0.5–2.0 Gm. three times daily. All the tetracyclines, chloramphenicol and erythromycin have been used without further therapeutic advantage. The protection of the host against invasion by antibiotic-resistant micro-organisms clearly depends on the maintenance of a leukocytic reaction in the colonic mucosa. It is therefore not surprising that the use of cortisone or corticotropin would be followed, in some instances, by perforation of the bowel and other untoward effects. The positive therapeutic advantages of these hormones are evaluated below.

NUTRITIONAL REPAIR.—Even in patients who have lost no weight, serious nutritional losses are usually evident, and repair of these is an important step in therapy. The stools carry away large quantities of tissue protein, as well as iron and vitamins. In the early stages these losses are easily compensated; and weight loss, anemia and hypoproteinemia do not usually develop until the appetite fails and intake of food is diminished. The disease has been treated with equal success with diets low in residue or normal in residue. It follows that encouragement of the patient to eat and provision of an appetizing, nutritionally liberal diet are more important to recovery than elimination of the trauma of food residues. Patients with ileus or signs of hyperacute inflammation may have to be maintained by parenteral means; a mixture of 5 per cent casein hydrolysate with dextrose and ethyl alcohol may be infused slowly by vein (1,000 cc. in three to four hours). In such cases the hemoglobin may be normal, but blood volume determination may show that the total red blood cell mass is low and that transfusions are indicated. Likewise, acute deficiencies of serum albumin and of serum potassium or other electrolytes should be recognized and corrected. Empirically, the known vitamins are supplied in amounts representing four or five times the daily requirement, though specific indications for their use may be lacking.

ROLE OF STEROID THERAPY.—Treatment with corticotropin or cortisone has been specifically credited, by many writers, with the relief of symptoms and signs of colitis in the vast majority of their

patients, even though their studies lacked suitable controls. Recently, therapy with cortisone has been subjected to a "double-blind test" by a group of English workers, and the results in those treated with the hormone were statistically superior to those obtained with the placebo, though not strikingly so. It seems probable that the therapeutic results ordinarily achieved may be due in some degree to the suppression of "toxemic" or hypersensitive phenomena related to the inflammation; more largely to the stimulation of appetite and elevation of mood; but most of all to the therapeutic enthusiasm of the physician. The use of corticotropin and cortisone should therefore be timed to take advantage of the rising tide of confidence of the patient in his physician, and confined to those patients with relatively indolent disease, who are not progressing satisfactorily after two or three weeks of intensive therapy by more conservative measures. The use of these agents in patients with fulminating colitis is a calculated risk with many unknown factors, and one which I am seldom willing to assume.

INDICATIONS FOR SURGERY.—The need for surgical intervention in local complications of colitis, such as severe hemorrhage, perforation, carcinoma or obstruction, requires no comment. The difficult decisions involve "medical intractability" and the risk of cancer. A patient should hardly be judged intractable to medical management unless continuous medical therapy and supportive psychotherapy have been carried out over two years. In such a case, the patient's present disability should be conscientiously compared with the problems of management encountered by the average patient with an ileostomy. Thus, for nearly all those with five or more urgent bowel movements daily, social disability will be lessened by the operation. Finally, the problems of ileostomy management should be fairly presented to the patient, and an encouraging view given of the rehabilitation which is possible, perhaps by interview with patients of the same sex and social status who have adjusted well to their ileostomies. All these steps are advisable in anticipation of a purely elective operation. To the degree that the current status of the patient is a threat to his life, this procedure should be modified.

We know that the occurrence of carcinoma of the colon as a complication of ulcerative colitis is significantly more frequent than in the general population and that it usually develops after five or

more years of continuous inflammation. Further, it is clear that, because of the difficulty of identifying the symptoms of cancer in a patient already having bloody diarrhea, few patients undergo colectomy early enough to effect a cure. Although it is commonly believed that inflammatory pseudopolyposis is a specific precancerous change in ulcerative colitis, there is no convincing evidence that this or any other change in the mucosa will reliably indicate those patients in whom cancers will develop. We still lack adequate data by which to compare the risk of "prophylactic surgery" with the risk of death, at various ages, from carcinoma alone, although the higher risk in those developing colitis in early life seems established. Therefore, it is suggested that purely "prophylactic colectomy" be restricted to those whose colitis began before age 20 and has been continuously present (though not always symptomatic) for five or more years. Fortunately for the physician, the patients with the greater risk of carcinoma usually need colectomy for other reasons as well.

Regional Enteritis

This disease, identified less than 25 years ago by Crohn and his associates, is an extremely chronic granulomatous process of unknown etiology. While we await the results of more prolonged clinical observation and more conclusive studies of its pathogenesis, we should base our management upon certain well established facts of its pathology, pathologic physiology and natural history.

The site of predilection of the lesions of regional enteritis is the tunica propria and submucosa of the distal ileum. Passing through a sequence of changes, including lymphedema, lymphatic hyperplasia, secondary infection, necrosis and cicatrization, the process spreads to the outer coats of the intestine, the mesenteric lymphatic vessels and nodes, and occasionally to the liver. Adhesion of the inflamed bowel to adjacent structures (bowel, bladder, abdominal wall) may be followed by fistula formation. Extensions of the original process or separate lesions ("skip areas") usually appear in more proximal portions of the small intestine, rarely in the cecum and ascending colon.

The symptoms and signs of the disease bear a readily understandable relationship to these lesions. There is a large-stool *diarrhea,* often with occult bleeding, but rarely with gross blood or visible

pus or mucus. The *pain* is periumbilical or in the right lower quadrant, cramplike, associated with borborygmi, relieved often by vomiting. In periods of acute inflammation there are varying degrees of *fever,* leukocytosis and elevation of the sedimentation rate. The nutritional loss leads, as it does in sprue, to *weakness, fatigue, weight loss* and *delayed maturation* of children, especially if *anorexia* also develops.

The physical signs result largely from the fibrosis and fistula formation which characterize the late stage of pathogenesis. Intestinal obstruction may be manifested by *abdominal distention* and *audible peristalsis.* A *mass* is often felt, usually in the right lower quadrant, consisting of a chronically inflamed loop and adherent tissues. *Fistulous openings* may be found in the abdominal wall or perineum, or passage of gas and pus in the urine may signalize an enterovesical fistula. Anemia is often severe, of normocytic or microcytic type, and associated with striking *pallor. Edema* and *ascites* are usually related to lowered serum albumin.

The clinical diagnosis can be established only by x-ray. The barium enema is done first, omitting the castor oil preparation; and by its "ileal leak" a lesion of the terminal ileum is often revealed. The upper limit of the disease in the small bowel must be estimated by a barium meal with small intestinal films. Reflecting the pathology of the disease, the involved segments appear on x-ray to be narrowed, with a ragged mucosal surface and polypoid filling defects of various sizes. Proximally, the intestine is dilated and its motility delayed and irregular. Extreme narrowing of long segments of distal or terminal ileum produces the classic "string sign."

Variations in the pathology and natural history account for a number of clinical types, each with its separate differential diagnosis and prognostic import. *Acute ileitis,* for practical purposes clinically indistinguishable from acute appendicitis, leads one almost inevitably to perform an exploratory laparotomy. Complete and lasting spontaneous remission occurs in a majority of these cases. *Chronic terminal ileitis,* with its right lower quadrant mass and evidences of obstruction, must be differentiated from carcinoma of the cecum, appendiceal abscess, ileocecal tuberculosis or tumors of the ileum. The lesions almost never disappear spontaneously; rather, they progress to more severe obstruction or fistula formation. *Ileocolitis* may be impossible to distinguish from regional or

right-sided ulcerative colitis, except that on x-ray the latter disease does not show marked narrowing of the ileum. This process may also be considered irreversible, but the course is characterized less by obstruction than by diarrhea and fever. In *ileojejunitis* the leading clinical symptoms and signs are those of sprue; but, in addition, the patient usually has pain and fever, the leukocyte count is elevated and the small intestinal x-rays may show luminal narrowing and eccentric dilatations of various loops. Since this process is to a large degree a reversible one, considerable spontaneous improvement can be expected.

The natural history of regional enteritis is most often one of change, over a period of months or years, from a predominantly exudative subacute inflammation with ill-defined limits, to a well localized, fibrotic, extremely indolent process. Accordingly, the leading principle of therapy is to treat the early lesions medically, supporting the health of the patient until such time as the inflammation becomes quiescent and the residual scars can be dealt with, if need be, by surgery. Rest, relief of fatigue and tension, diet and vitamin supplementation are arranged in the manner suggested for ulcerative colitis, except that patients with ileitis are generally more mature and require less supportive psychotherapy. Patients with diffuse involvement of the small intestine often have severe nutritional deficiencies, and these can be treated as they are in patients with sprue (see below). Antibiotics and chemotherapy are of value in the presence of suspected secondary infection, or with fistula and abscess formation. For acute situations, intramuscular penicillin and streptomycin can be used; for chronic needs, sulfathalidine, in the dosage recommended for ulcerative colitis. Cortisone and corticotropin find a rational place in the management of this relatively indolent inflammation and have caused relatively few untoward effects. While they cannot arrest the disease, they may tide the patient over an otherwise exhausting and dangerous episode. Oral cortisone is most often used, 300 mg. being given the first day, 100 mg. per day for the next three weeks, then a minimum maintenance dose for a prolonged course.

The best indications for surgery are obstruction and fistula formation. The operation should include complete transection of the small intestine above the highest recognizable lesion, and end-to-side anastomosis with the highest available segment of the colon

(usually the midtransverse colon). In and proximal to the area of the anastomosis, about one out of five patients will develop a recurrence of disease, usually within four to six years.

Steatorrhea

Among the patients with large-stool diarrhea, a significant number pass excessively bulky stools which are pale, foul, and greasy or fatty in appearance. This clinical phenomenon, steatorrhea, is confirmed by chemical analysis if fat constitutes 25 per cent or more of the dry weight of the stools, or over 4 per cent of the measured dietary intake of fat. This excess may result from defects either of digestion or of absorption of fat.

Digestive defect—pancreatogenous steatorrhea.—Since the only important lipase in human digestion is that of the pancreas, and as resection of all but a small remnant of this organ is compatible with normal digestion of fat, defective fat splitting usually implies advanced disease of the pancreas. In the infant and child, this is usually due to congenital cystic fibrosis (mucoviscidosis). In the adult, the problem occurs more rarely and is associated with chronic pancreatitis, pancreatic cancer and previous total pancreatectomy. In the absence of pancreatic destruction, defective digestion of fat may be related to poor emulsification within the bowel, as in the presence of complete biliary obstruction, or rarely to inefficient exposure of food to pancreatic juice, as after gastrectomy or other short-circuiting operations.

The diagnostic impression of pancreatogenous steatorrhea, suggested by symptoms and clinical signs of one of the above conditions, can be supported in various ways. Further evidence of diffuse pancreatic damage may be found in an oral glucose tolerance curve of diabetic configuration, or in a flat plate of the abdomen, showing calcification of the pancreas. The starch tolerance test of Althausen, in which blood sugar levels after the ingestion of glucose are compared with those after an equal amount of starch, may prove to be a convenient and reliable index of digestive capacity. Chemical determinations of excess nitrogen in the stools and of a high ratio of neutral fat to free fatty acids and soaps are not conclusive evidence of a digestive defect, as opposed to an absorptive defect. The most satisfactory evidence of pancreatic insufficiency is a

grossly abnormal secretin test, performed by experienced hands. The most convenient and generally available evidence is a clinical trial of pancreatin.

Properly used, substitution therapy with pancreatic extracts is highly effective. At least 3.6 Gm. of USP pancreatin should be taken during each meal; this will require 36 of the standard 0.3 Gm. tablets daily, or smaller quantities of more concentrated extracts. When defective pancreatic digestion is a major cause of steatorrhea, the patient's weight should rise and his stools decrease in number and size within 10 days after beginning such therapy.

ABSORPTIVE DEFECT—SPRUE.—Failure of absorption of fat and other foodstuffs at once suggests an anatomical or functional abnormality of the small intestine. This may be due to gross defects, such as those resulting from massive resection of the small bowel for mesenteric thrombosis, or to shortened intestinal transit time, as in the dumping syndrome or a gastrojejunocolic fistula. Rarely does it result from extensive involvement of the small intestinal mucosa, submucosa and mesenteric lymphatics by chronic infections or neoplastic disease. Regional enteritis, and more rarely tuberculous enteritis, may manifest themselves first by steatorrhea. Lymphosarcoma may develop in this manner, the intestinal symptoms antedating by a year or more the findings of generalized disease. In intestinal lipodystrophy, or Whipple's disease, the sprue syndrome is associated with fever, adenopathy, arthritis, polyserositis and chronic cough. Much more commonly, such an absorptive defect occurs in the absence of any morphologic change in the bowel indicating the cause of the process; this is called *sprue, idiopathic steatorrhea* or, in children, *celiac disease.*

The syndrome of sprue, though complex and not wholly explained, can be related in most of its particulars to well established physiologic disturbances. The *steatorrhea* reflects the failure of absorption of the end products of fat digestion, including fatty acids and soaps, and their consequent accumulation in the bowel, enlarging the stool by osmotic activity and chemically irritating the mucosa. This loss, together with the delayed absorption of glucose from the intestine, accounts for a good deal of the *weight loss* and, indirectly through wastage of protein, for the *emaciation, hypoproteinemia* and, to some extent, the *anemia.* More important causes of the anemia are the failure of absorption of the erythrocyte

maturation factor (even though the patient has intrinsic factor and an adequate intake of vitamin B_{12}) and the losses of iron. Conditioned deficiencies of other B complex factors appear related to the *lesions of the mucous membranes,* especially glossitis and the aphthous ulcers of the mouth, from which the condition derives its name (*sprouw* is Dutch for "aphthous ulcer"). Clinical signs of vitamin A deficiency are rarely seen, although impairment of absorption of this vitamin, as measured by a failure of its plasma concentration to rise after its oral administration, is commonly used to document the general absorptive defect. Significant losses of vitamin K are not infrequent, resulting in hypoprothrombinemia and *hemorrhagic phenomena,* which cease on parenteral injection of small amounts of synthetic naphthoquinones. *Hypocalcemia* with latent or manifest *tetany* commonly occurs, due in part to poor absorption of vitamin D and in part to losses of calcium through formation of insoluble calcium soaps in the lumen of the bowel. Despite the magnitude of these losses of calcium, only in children is the skeleton seriously demineralized.

In addition to these defects of absorption, there is a marked disturbance of motility of the small intestine. This is manifested roentgenologically by delay in the passage of a barium meal, discontinuous motility resulting in clumping or "puddling" of the contrast medium, increased diameter of the loops and blunting and diminution in number of the mucosal folds. At the bedside, one sees *distension* of the abdomen, characteristically increasing in severity from breakfast to bedtime, worse when diarrhea is more severe, and aggravated by fatty food. This pattern of motility disturbance, in which large quantities of gas and fluid are retained in the bowel during the day but resorbed during the night, is regarded as the cause of the *nocturia* experienced by many of these patients.

The pattern of symptoms varies greatly in specific patients, as does the natural history of the disease. Most noteworthy is the occurrence of these multiple signs of deficiency in the absence of diarrhea; in such cases, the steatorrhea has been established purely by chemical analysis of the stools. In the tropics and in other areas where malnutrition is prevalent, sprue commonly appears acutely as an almost epidemic disease, is manifested often by mouth lesions and macrocytic anemia and goes into prompt remission with dietotherapy plus vitamin B_{12} or liver extract. In the temperate zone

the syndrome more often develops sporadically and insidiously in persons whose nutritional intake has been good; it is more commonly manifested by tetany than by macrocytic anemia, and it is slowly and usually incompletely relieved by conventional therapy. These two types are often called *tropical sprue* and *nontropical sprue,* respectively. They probably represent the extreme ends of a spectrum, between which many intermediate clinical patterns are possible.

Current therapy of sprue is basically an attempt to compensate past and present nutritional losses by a careful program of hyperalimentation. For initial control of the steatorrhea, dietary fat is reduced to a minimum and caloric requirements are made up by proteins and carbohydrates. The diet may be of normal residue. In long term management, it is preferable to restore moderate amounts of fat to the diet, permitting some diarrhea, in order to achieve optimum weight and general nutritional status. Basic mineral and vitamin requirements are best met by including large amounts of meat, skim milk and fresh vegetables and by providing five to ten times the usual daily requirement of the known vitamins, in the form of multivitamin capsules, drops or syrups.

This basic regimen must be reinforced by further supplementation whenever outstanding deficiencies are revealed by specific clinical or laboratory findings. Megaloblastic or macrocytic anemia may respond to parenteral vitamin B_{12} (15μg. per day at first) or to intramuscular liver extract (4–30 units per day). Rarely, the anemia is resistant to these agents, but is relieved by folic acid 30–100 mg. per day. Microcytic anemia may improve on oral iron, as with ferrous sulfate 0.4–0.6 Gm. three times daily, one hour before meals; or may require carefully calculated parenteral therapy with saccharated iron oxide. Hypocalcemia should be treated with enormous oral doses of calcium (for example, calcium lactate 1.2–3.0 Gm. four times daily) and vitamin D (as much as 4,000,000 units daily to raise the serum calcium level to normal and 1,200,000 units daily to maintain it). The danger of vitamin D intoxication depends upon hypercalcemia; therefore, the serum calcium is determined at least weekly at first, and every one to three months during maintenance on an established regimen. Hypoprothrombinemia usually responds promptly to one or two daily intramuscular injections of 2–4 mg. of synthetic 2–methyl–1, 4–naphthoquinone;

further dosage can be guided by repeated prothrombin determinations.

In cases refractory to the above therapy, trial of two other measures can today be recommended. *Cortisone* can be given orally, beginning with 50–75 mg. every six hours, reduced gradually over four weeks' time to a maintenance level of 30–75 mg. per day. Documented results include increase in appetite and weight, reduction of diarrhea, improvement in x-ray signs in the small bowel, better absorption of vitamin A and improved absorption of fat in metabolic balance studies. In successful cases the benefits are usually obvious within a week. If effective, steroid therapy should be continued for six months or longer, then terminated in a hospital with a course of corticotropin to reawaken the idle adrenal glands.

The recent discovery of the effectiveness of the *gluten-free diet* in some cases of celiac disease and sprue has aroused wide interest, and it is suggested that all but the mildest cases be given a thorough trial on this regimen. This diet is restricted only in the complete exclusion of all sources of gluten (wheat and rye products of all kinds), and normal amounts of fat are permitted from the beginning. The value of this diet has been affirmed by fat balance studies in children with celiac disease. In adults its use is supported by less satisfactory evidence, but uncontrolled clinical studies indicate complete relief of the syndrome within two to three weeks in certain cases of sprue, with little or no benefit in others. Even if no other evidence were available, this should indicate to us that the entity we call "idiopathic steatorrhea" probably is still heterogeneous, including a number of disorders of differing etiology.

Postgastrectomy Dumping Syndrome—Osmotic Diarrhea

Recent studies on patients with the dumping syndrome after total or subtotal gastrectomy have yielded not only a better understanding of this interesting mechanism of diarrhea but a basis for more rational and effective therapy.

This condition is recognized clinically by the typical symptoms developing in a gastrectomized patient, usually at the time full oral feedings are resumed following operation. From 5 to 20 minutes after eating, the patient may suddenly feel weak and faint, sweat

profusely and experience severe palpitation and midabdominal griping or cramping pain. Less commonly, headache, nausea and vomiting may occur. Two to three hours later, he may experience sudden hunger, again feel weak, and perspire profusely, as with an insulin reaction. During the day, he may have two or more bulky, watery or greasy stools. These have been found, on chemical analysis, sometimes to contain excess fat. Any one of these manifestations, including diarrhea, may be the chief complaint. The patient usually will have noticed that lying down will relieve his early shocklike symptoms, that the syndrome is worse after larger meals or even that sweets will aggravate the symptoms. This condition can readily be distinguished from gastrojejunocolic fistula by the details of the history. The latter condition can usually be demonstrated by a barium enema.

The dumping syndrome has been experimentally reproduced, both in gastrectomized patients and in healthy persons, by the sudden introduction of hypertonic fluids (by way of an intestinal tube) directly into the upper jejunum. Hypertonic glucose, for example, is immediately diluted by diffusion of extracellular fluids through the wall of the intestinal loop. The volume of circulating plasma, as measured by the dye method, may diminish by 25 per cent in only a few minutes; thus, the shocklike state becomes quite understandable. The sudden effusion of fluid into the gut initiates a peristaltic rush, and the small intestine is traversed too rapidly for adequate absorption; this is one apparent reason for the diarrhea. One substance which usually is well absorbed is glucose, and the brief period of its absorption leads to a sudden rise and later a sudden fall of blood sugar, thus simulating insulin shock.

The experimental results indicate that these changes develop readily on instillation of sugars in concentrations commonly eaten and that soluble or suspended starches have an equal or greater effect, probably because of rapid digestion to sugars. Proteins and fats, however, are digested so slowly as to have relatively little osmotic influence. Hence, patients with the dumping syndrome should be fed a high protein, high fat, low carbohydrate diet, given in six small, relatively dry feedings each day. Supplementary fluid should be taken shortly before eating, when its flushing action will be less of a disadvantage.

Postantibiotic Diarrhea

The occurrence of diarrhea as an unfavorable effect of broad spectrum antibiotics has been widely noted. The greatest emphasis has been placed on the development of acute pseudomembranous enterocolitis in postoperative patients, apparently due in part to the emergence of an antibiotic-resistant strain of Micrococcus pyogenes aureus.

Chronic diarrhea has also been observed to occur after as little as one or two days of therapy with one of the tetracycline compounds, and may last as long as two years. These patients usually have no impressive physical signs except weight loss, which may be moderately severe. The rectal and sigmoid mucosa, when visualized by endoscopy, often appears diffusely hyperemic and velvety, with whitish dry exudate very much like a pseudomembrane. The stools are large and watery, with undigested food particles and a foul ammoniacal odor. This is probably produced by the organism which usually predominates on culture, Proteus vulgaris. Monilia may also be abundant, and other resistant organisms found in lesser numbers. In every case of this syndrome the fecal flora are radically altered, and the final disappearance of symptoms has often been seen to coincide with the return of the fecal organisms to normal distribution.

Despite great differences in the duration of illness, this process appears to be self-limited, and so a variety of therapeutic measures have been credited with success. In severe and prolonged cases, all means of therapy used—such as vitamins, anticholinergic drugs, erythromycin and other less common antibiotics and implantation of Lactobacillus acidophilus—have been fruitless. Until further light is shed on the etiology of this stubborn iatrogenic disease, the patients may best be treated symptomatically by binding agents and by restoration of losses of fluid and electrolytes.

CONCLUSION

It is to be confidently expected that continued progress in our knowledge of the mechanisms of chronic and recurrent diarrhea will soon render obsolete many features of this review. It is hoped that the physiological concepts here presented may permit the

ready incorporation of newer knowledge in this field. The physician, nevertheless, will still be required to draw on his clinical resourcefulness to fulfil his threefold obligation to the patient with diarrhea: first, to detect serious underlying organic disease, chiefly carcinoma of the colon; second, to relieve the distress and disability that diarrhea produces, whatever its cause; and third, to recognize that it frequently is a symptom of difficult adaptation to stress, requiring treatment broadly directed at the whole personality.

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